Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-13. (Canceled)

14. (Currently amended) A method for determining a probability that an expression level of a cellular constituent in a plurality of paired differential microarray experiments is altered by a perturbation, wherein each paired differential microarray experiment in said plurality of paired differential microarray experiments comprises a first microarray experiment representing a baseline state of a first biological system, and a second microarray experiment representing a perturbed state of said first biological system, said method comprising the steps of

(a) determining an error distribution statistic by fitting a reference pair of microarray experiments with an intensity independent statistic, wherein said reference pair of microarray experiments comprises a first reference microarray experiment, and a second reference microarray experiment that is a nominal repeat of said first reference microarray experiment according to a formula

$$\frac{(X-Y)}{\sqrt{\sigma_X{}^2+\sigma_Y{}^2+f^2(X^2+Y^2)}}$$

where

X represents an intensity of said cellular constituent in said first reference microarray experiment,

Y represents an intensity of said cellular constituent in said second reference microarray experiment,

$\sigma_X{}^2$ is a variance term for X that represents an additive error level in X,

$\sigma_Y{}^2$ is a variance term for Y that represents an additive error level in Y, and

f is a fractional multiplicative error level;

(b) determining, for each paired differential microarray experiment in said plurality of paired differential microarray experiments, an amount of change in expression level of said cellular constituent between the second microarray experiment and the first microarray experiment of said paired differential microarray experiment using said error distribution statistic; and

(c) determining said probability that said expression level of said cellular constituent in said plurality of paired differential microarray experiments is altered by said perturbation by combining, for each paired differential microarray experiment in said plurality of paired differential microarray experiments, each amount of change in expression level of said cellular constituent determined in step (b) using a rank based method comprising:

$$P(H_0^+) = \prod_i P_i \text{ or}$$

$$P(H_0^-) = \prod_i (1 - P_i)$$

where

P_i is the percentile rank of the expression of said cellular constituent in the i^{th} pair of paired differential microarray experiments in said plurality of paired differential microarray experiments,

$P(H_0^+)$ is the chance that said cellular constituent is not up-regulated in said plurality of paired differential microarray experiments, and

$P(H_0^-)$ is the chance that said cellular constituent is not down-regulated in said plurality of paired differential microarray experiments.

15. (Currently amended) A computer system for determining a probability that an expression level of a cellular constituent in a plurality of paired differential microarray experiments is altered by a perturbation, wherein each paired differential microarray experiment in said plurality of paired differential microarray experiments comprises a first microarray experiment representing a baseline state of a first biological system, and a second microarray experiment representing a perturbed state of said first biological system; the computer system comprising a processor, and a memory encoding one or more programs coupled to the processor and the one or more programs cause the processor to perform a method comprising the steps of

(a) determining an error distribution statistic by fitting a reference pair of microarray experiments with an intensity independent statistic, wherein said reference pair of microarray experiments comprises a first reference microarray experiment, and a second reference microarray experiment that is a nominal repeat of said first reference microarray experiment according to a formula

$$\frac{(X-Y)}{\sqrt{\sigma_X{}^2+\sigma_Y{}^2+f^2(X^2+Y^2)}}$$

where

X represents an intensity of said cellular constituent in said first reference microarray experiment,

Y represents an intensity of said cellular constituent in said second reference microarray experiment,

$\sigma_X{}^2$ is a variance term for X that represents an additive error level in X,

$\sigma_Y{}^2$ is a variance term for Y that represents an additive error level in Y, and

f is a fractional multiplicative error level;

(b) determining, for each paired differential microarray experiment in said plurality of paired differential microarray experiments, an amount of change in expression level of said cellular constituent between the second microarray experiment and the first microarray experiment using said error distribution statistic; and

(c) determining said probability that said expression level of said cellular constituent in said plurality of paired differential microarray experiments is altered by said perturbation by combining, for each paired differential microarray experiment in said plurality of paired differential microarray experiments, each amount of change in expression level of said cellular constituent determined in step (b) using a rank based method comprising:

$$P(H_0^+)=\prod_i P_i \text{ or}$$

$$P(H_0^-)=\prod_i (1-P_i)$$

where

P_i is the percentile rank of the expression of said cellular constituent in the i^{th} pair of paired differential microarray experiments in said plurality of paired differential microarray experiments,

$P(H_0^+)$ is the chance that said cellular constituent is not up-regulated in said plurality of paired differential microarray experiments, and

$P(H_0^-)$ is the chance that said cellular constituent is not down-regulated in said plurality of paired differential microarray experiments.

16 - 19. (Canceled)

20. (Previously presented) The method of Claim 14 wherein said rank based method determines a probability that said cellular constituent is up-regulated in response to a perturbation.

21. (Previously presented) The computer system of Claim 15 wherein said rank based method determines a probability that said cellular constituent is up-regulated in response to a perturbation.

22. (Canceled)

23. (Previously presented) The method of Claim 14 wherein said rank based method determines a probability that said cellular constituent is down-regulated in response to said perturbation.

24. (Canceled)

25. (Previously presented) The method of Claim 14 wherein each paired differential microarray experiment in said plurality of paired differential microarray experiments is a two-fluorophore microarray experiment wherein a first fluorophore represents said baseline state of said biological system and a second fluorophore, distinguishable from said first fluorophore, represents said perturbed state of said biological system.

26. (Previously presented) The method of Claim 14 wherein a single fluorophore is used in each said paired differential microarray experiments in said plurality of paired differential microarray experiments.

27. (Previously presented) The method of Claim 14 wherein a first fluorophore is used in said first reference microarray experiment and a second fluorophore, distinguishable from said first fluorophore, is used in said second reference microarray experiment.

Claims 28-42. (Canceled)

43. (Previously presented) The method of Claim 14 wherein said perturbed state of said first biological system is achieved by a method comprising exposing said first biological system, when representing said baseline state, to a pharmacological agent.

44. (Previously presented) The computer system of Claim 15 wherein said perturbed state of said first biological system is achieved by a method comprising exposing said first biological system, when representing said baseline state, to a pharmacological agent.

45. (Withdrawn) The method of Claim 14 wherein said perturbed state of said first biological system is achieved by a method comprising exposing said first biological system, when representing said baseline state, to a drug candidate.

46. (Withdrawn) The computer system of Claim 15 wherein said perturbed state of said first biological system is achieved by a method comprising exposing said first biological system, when representing said baseline state, to a drug candidate.

47. (Withdrawn) The method of Claim 14 wherein said perturbed state of said first biological system is achieved by a method comprising introducing an exogenous gene into said first biological system.

48. (Withdrawn) The computer system of Claim 15 wherein said perturbed state of said first biological system is achieved by a method comprising introducing an exogenous gene into said first biological system.

49. (Withdrawn) The method of Claim 14 wherein said perturbed state of said first biological system is achieved by a method comprising deleting a gene from said first biological system.

50. (Withdrawn) The computer system of Claim 15 wherein said perturbed state of said first biological system is achieved by a method comprising deleting a gene from said first biological system.

51. (Withdrawn) The method of Claim 14 wherein said perturbed state of said first biological system is achieved by a method comprising changing a culture condition of said first biological system.

52. (Withdrawn) The computer system of Claim 15 wherein said perturbed state of said first biological system is achieved by a method comprising changing a culture condition of said first biological system.

53. (Withdrawn) The method of Claim 14 wherein said perturbed state of said first biological system is due to the onset of a disease in said first biological system.

54. (Withdrawn) The computer system of Claim 15 wherein said perturbed state of said first biological system is due to the onset of a disease in said first biological system.

55. (Previously presented) The method of Claim 14 wherein said first biological system is a cell line, a cell culture, a tissue sample, an organ, or a multicellular organism.

56. (Previously presented) The computer system of Claim 15 wherein said first biological system is a cell line, a cell culture, a tissue sample, an organ, or a multicellular organism.

57. (Previously presented) The method of Claim 14 wherein said first biological system is a mammal.

58. (Previously presented) The computer system of Claim 15 wherein said first biological system is a mammal.

59. (Previously presented) The method of Claim 14 wherein said first biological system is a *Homo sapien.*

60. (Previously presented) The computer system of Claim 15 wherein said first biological system is a *Homo sapien.*

61. (Withdrawn) The method of Claim 14 wherein said first biological system is a yeast that is substantially isogenic to *Saccharomyces cerevisia.*

62. (Withdrawn) The computer system of Claim 15 wherein said first biological system is a yeast that is substantially isogenic to *Saccharomyces cerevisia.*

63. (Previously presented) The method of Claim 14 wherein said baseline state represents the wild-type state of said first biological system.

64. (Previously presented) The computer system of Claim 15 wherein said baseline state represents the wild-type state of said first biological system.

65. (Previously presented) The method of Claim 14 wherein said baseline state represents a different perturbed state of said first biological system.

66. (Previously presented) The computer system of Claim 15 wherein said baseline state represents a different perturbed state of said first biological system.

67. (Previously presented) The method of Claim 14 wherein each said first microarray experiment and each said second microarray experiment in each paired differential microarray experiment in said plurality of paired differential microarray experiments uses a microarray having binding sites corresponding to at least fifty percent of the genes in the genome of said first biological system, and wherein said first biological system is a cell or a multicellular organism.

68. (Previously presented) The computer system of Claim 15 wherein each said first microarray experiment and each said second microarray experiment in each paired differential microarray experiment in said plurality of paired differential microarray experiments uses a microarray having binding sites corresponding to at least fifty percent of the genes in the genome of said first biological system, and wherein said first biological system is a cell or a multicellular organism.

69. (Previously presented) The method of Claim 14 wherein each said first microarray experiment and each said second microarray experiment in each paired differential microarray experiment in said plurality of paired differential microarray experiments uses a microarray having binding sites corresponding to at least seventy-five percent of the genes in the genome of said first biological system, and wherein said first biological system is a cell or a multicellular organism.

70. (Previously presented) The computer system of Claim 15 wherein each said first microarray experiment and each said second microarray experiment in each paired differential microarray experiment in said plurality of paired differential microarray experiments uses a microarray having binding sites corresponding to at least seventy-five percent of the genes in the genome of said first biological system, and wherein said first biological system is a cell or a multicellular organism.

71. (Previously presented) The method of Claim 14 wherein each said first microarray experiment and each said second microarray experiment in each paired differential microarray experiment in said plurality of paired differential microarray experiments uses a microarray having binding sites corresponding to at least eighty-five percent of the genes in the genome of said first biological system, and wherein said first biological system is a cell or a multicellular organism.

72. (Previously presented) The computer system of Claim 15 wherein each said first microarray experiment and each said second microarray experiment in each paired differential microarray experiment in said plurality of paired differential microarray experiments uses a microarray having binding sites corresponding to at least eighty-five percent of the genes in the genome of said first biological system, and wherein said first biological system is a cell or a multicellular organism.

73. (Previously presented) The method of Claim 14 wherein each said first microarray experiment and each said second microarray experiment in each paired differential microarray experiment in said plurality of paired differential microarray experiments uses a microarray having binding sites corresponding to at least ninety percent of the genes in the genome of said first biological system, and wherein said first biological system is a cell or a multicellular organism.

74. (Previously presented) The computer system of Claim 15 wherein each said first microarray experiment and each said second microarray experiment in each paired differential microarray experiment in said plurality of paired differential microarray experiments uses a microarray having binding sites corresponding to at least ninety percent of the genes in the genome of said first biological system, and wherein said first biological system is a cell or a multicellular organism.

75. (Previously presented) The method of Claim 14 wherein each said first microarray experiment and each said second microarray experiment in each paired differential microarray experiment in said plurality of paired differential microarray experiments uses a microarray having binding sites corresponding to at least ninety-nine percent of the genes in the genome of said first biological system, and wherein said first biological system is a cell or a multicellular organism.

76. (Previously presented) The computer system of Claim 15 wherein each said first microarray experiment and each said second microarray experiment in each paired differential microarray experiment in said plurality of paired differential microarray experiments uses a microarray having binding sites corresponding to at least ninety-nine percent of the genes in the genome of said first biological system, and wherein said first biological system is a cell or a multicellular organism.

77. (Previously presented) The method of Claim 25 wherein said first fluorophore and said second fluorophore are selected from the group consisting of Cy2-deoxynucleotide triphosphate, Cy3-deoxynucleotide triphosphate, Cy3.5-deoxynucleotide triphosphate, Cy5-deoxynucleotide triphosphate, Cy5.5-deoxynucleotide triphosphate, Cy7-deoxynucleotide triphosphate, fluorescein, lissamine, phycoerythrin, and rhodamine.

78. (Previously presented) The method of Claim 26 wherein said single fluorophore is selected from the group consisting of Cy2-deoxynucleotide triphosphate, Cy3-deoxynucleotide triphosphate, Cy3.5-deoxynucleotide triphosphate, Cy5-deoxynucleotide triphosphate, Cy5.5-deoxynucleotide triphosphate, Cy7-deoxynucleotide triphosphate, fluorescein, lissamine, phycoerythrin, and rhodamine.

79. (Previously presented) The computer system of Claim 15 wherein each paired differential microarray experiment in said plurality of paired differential microarray experiments is a two-fluorophore microarray experiment wherein a first fluorophore represents said baseline state of said first biological system and a second fluorophore, distinguishable from said first fluorophore, represents said perturbed state of said first biological system.

80. (Previously presented) The computer system of Claim 79 wherein said first fluorophore and said second fluorophore are selected from the group consisting of Cy2-deoxynucleotide triphosphate, Cy3-deoxynucleotide triphosphate, Cy3.5-deoxynucleotide triphosphate, Cy5-deoxynucleotide triphosphate, Cy5.5-deoxynucleotide triphosphate, Cy7-deoxynucleotide triphosphate, fluorescein, lissamine, phycoerythrin, and rhodamine.

81. (Previously presented) The computer system of Claim 15 wherein a single fluorophore is used in said paired differential microarray experiments.

82. (Previously presented) The computer system of Claim 81 wherein said single fluorophore is selected from the group consisting of Cy2-deoxynucleotide triphosphate, Cy3-deoxynucleotide triphosphate, Cy3.5-deoxynucleotide triphosphate, Cy5-deoxynucleotide triphosphate, Cy5.5-deoxynucleotide triphosphate, Cy7-deoxynucleotide triphosphate, fluorescein, lissamine, phycoerythrin, and rhodamine.

83-94. (Canceled)

95. (New) A method of estimating a significance *d* in a difference between a measurement of a cellular constituent in a first microarray experiment and a measurement of the cellular constituent in a second microarray experiment comprising computing:

$$d = \frac{(X - Y)}{\sqrt{\sigma_X^{\,2} + \sigma_Y^{\,2} + f^2(X^2 + Y^2)}}$$

wherein

X is a brightness of a probe spot representing said cellular constituent in said first microarray experiment;

Y is a brightness of a probe spot representing said cellular constituent in said second microarray experiment;

σ_X^2 is a variance term for X that represents an additive error level in X;

σ_Y^2 is a variance term for Y that represents an additive error level in Y;

f is a fractional multiplicative error level;

$\sigma_X^2 + f^2X^2$ is an estimated variance for X; and

$\sigma_Y^2 + f^2Y^2$ is an estimated variance for Y.

96. (New) The method of Claim 95, wherein the first microarray experiment and the second microarray experiment are performed on the same microarray.

97. (New) The method of Claim 95, wherein the first microarray experiment and the second microarray experiment are each performed on a different microarray.

98. (New) The method of Claim 95, wherein

the first microarray experiment is repeated a number of times and the brightness of the probe spot X representing said cellular constituent in the first microarray experiment and each of the repeats of the first microarray experiment are combined to form a weighted mean x;

the second microarray experiment is repeated said number of times and the brightness of the probe spot Y representing said cellular constituent in the second microarray experiment and each of the repeats of the second microarray experiment are combined to form a weighted mean y;

wherein

$$d = \frac{(x - y)}{\sqrt{\sigma_X{}^2 + \sigma_Y{}^2 + f^2(x^2 + y^2)}},$$

and wherein

$$x = \frac{\sum \frac{x_i}{\sigma_{xi}^2}}{\sum\left(\frac{1}{\sigma_{xi}^2}\right)} \text{ and } y = \frac{\sum \frac{y_i}{\sigma_{yi}^2}}{\sum\left(\frac{1}{\sigma_{yi}^2}\right)},$$

$$\sigma_{xi}^2 = \sigma_X{}^2 + f^2X^2 \text{ and } \sigma_{yi}^2 = \sigma_Y{}^2 + f^2Y^2,$$

and wherein when said number of times approaches zero

$$\sigma_x \text{ approaches } \sqrt{\frac{1}{\sum\left(\frac{1}{\sigma_{xi}^2}\right)}}, \text{ and } \sigma_y \text{ approaches } \sqrt{\frac{1}{\sum\left(\frac{1}{\sigma_{yi}^2}\right)}},$$

and when said number of times approaches a large number

σ_x approaches observed error from scatter in X, and

σ_y approaches observed error from scatter in Y.

99. (New) The method of Claim 95 wherein said second microarray experiment is a nominal repeat of said first microarray experiment.

100. (New) The method of Claim 95 wherein said first microarray experiment represents a baseline state of a biological system and said second microarray experiment represents a perturbed state of said biological system.

101. (New) The method of Claim 100 wherein the perturbed state of said biological system is achieved by exposing said biological system, when representing said baseline state, to a pharmacological agent.

102. (New) The method of Claim 100 wherein the perturbed state of said biological system is achieved by exposing said first biological system, when representing said baseline state, to a drug candidate.

103. (New) The method of Claim 100 wherein the perturbed state of said biological system is achieved by introducing an exogenous gene into the biological system when the biological system represents said baseline state.

104. (New) The method of Claim 100 wherein said perturbed state of said biological system is achieved by deleting a gene from said biological system when the biological system represents said baseline state.

105. (New) The method of Claim 100 wherein said perturbed state of said biological system is achieved by changing a culture condition of said biological system when the biological system represents said baseline state.

106. (New) The method of Claim 100 wherein said perturbed state of said biological system is due to the onset of a disease in said biological system.

107. (New) The method of Claim 100 wherein the biological system is a cell line, a cell culture, a tissue sample, an organ, or a multicellular organism.

108. (New) The method of Claim 100 wherein the biological system is a mammal.

109. (New) The method of Claim 100 wherein the biological system is a *Homo sapien.*

110. (New) The method of Claim 100 wherein the biological system is a yeast that is substantially isogenic to *Saccharomyces cerevisia.*

111. (New) The method of Claim 100 wherein the baseline state represents the wild-type state of the biological system.

112. (New) The method of Claim 100 wherein the baseline state represents a different perturbed state of the biological system.

113. (New) A method of estimating a significance *d* in a difference between a measurement of a cellular constituent in a first microarray experiment and a measurement of the cellular constituent in a second microarray experiment comprising computing:

$$d = \frac{(X - Y)}{\sigma_{X\text{-}Y}}$$

wherein

X is a brightness of a probe spot representing said cellular constituent in said first microarray experiment;

Y is a brightness of a probe spot representing said cellular constituent in said second microarray experiment; and

$\sigma_{X\text{-}Y}$ is the combined error in the measurement of said cellular constituent in said first microarray experiment and the measurement of said cellular constituent in said second microarray experiment.

114. (New) The method of Claim 113, wherein the first microarray experiment and the second microarray experiment are performed on a single microarray.

115. (New) The method of Claim 113, wherein the first microarray experiment and the second microarray experiment are each performed on a different microarray.

116. (New) The method of Claim 113, wherein

the first microarray experiment is repeated a number of times and the brightness of the probe spot X representing said cellular constituent in the first microarray experiment and each of the repeats of the first microarray experiment are combined to form a weighted mean x;

the second microarray experiment is repeated said number of times and the brightness of the probe spot Y representing said cellular constituent in the second microarray experiment and each of the repeats of the second microarray experiment are combined to form a weighted mean y;

wherein

$$d = \frac{(x - y)}{\sigma_{X\text{-}Y}}$$

and

$$\sigma_{X\text{-}Y} = \sqrt{\sigma_X^2 + \sigma_Y^2}$$

and wherein

$$x = \frac{\sum \frac{x_i}{\sigma_{xi}^2}}{\sum\left(\frac{1}{\sigma_{xi}^2}\right)} \text{ and } y = \frac{\sum \frac{y_i}{\sigma_{yi}^2}}{\sum\left(\frac{1}{\sigma_{yi}^2}\right)},$$

and wherein when said number of times approaches zero

$$\sigma_x \text{ approaches } \sqrt{\frac{1}{\sum\left(\frac{1}{\sigma_{xi}^2}\right)}}, \text{ and } \sigma_y \text{ approaches } \sqrt{\frac{1}{\sum\left(\frac{1}{\sigma_{yi}^2}\right)}},$$

and when said number of times approaches a large number

σ_x approaches observed error from scatter in X, and

σ_y approaches observed error from scatter in Y.

117. (New) The method of Claim 116 wherein said second microarray experiment is a nominal repeat of said first microarray experiment.

118. (New) The method of Claim 116 wherein said first microarray experiment represents a baseline state of a biological system and said second microarray experiment represents a perturbed state of said biological system.

119. (New) The method of Claim 118 wherein the perturbed state of said biological system is achieved by exposing said biological system, when representing said baseline state, to a pharmacological agent.

120. (New) The method of Claim 118 wherein the perturbed state of said biological system is achieved by exposing said first biological system, when representing said baseline state, to a drug candidate.

121. (New) The method of Claim 118 wherein the perturbed state of said biological system is achieved by introducing an exogenous gene into the biological system when the biological system represents said baseline state.

122. (New) The method of Claim 118 wherein said perturbed state of said biological system is achieved by deleting a gene from said biological system when the biological system represents said baseline state.

123. (New) The method of Claim 118 wherein said perturbed state of said biological system is achieved by changing a culture condition of said biological system when the biological system represents said baseline state.

124. (New) The method of Claim 118 wherein said perturbed state of said biological system is due to the onset of a disease in said biological system.

125. (New) The method of Claim 118 wherein the biological system is a cell line, a cell culture, a tissue sample, an organ, or a multicellular organism.

126. (New) The method of Claim 118 wherein the biological system is a mammal.

127. (New) The method of Claim 118 wherein the biological system is a *Homo sapien.*

128. (New) The method of Claim 118 wherein the biological system is a yeast that is substantially isogenic to *Saccharomyces cerevisia.*

129. (New) The method of Claim 118 wherein the baseline state represents the wild-type state of the biological system.

130. (New) The method of Claim 118 wherein the baseline state represents a different perturbed state of the biological system.

131. (New) A method of determining an error σ_x of a weighted mean x for a quantitative measurement of a cellular constituent, the method comprising:

obtaining a plurality of instances N of said quantitative measurement, wherein each instance x_i of said quantitative measurement is from a first microarray experiment or a nominal repeat of said first microarray experiment;

computing

$$x = \frac{\sum \frac{x_i}{\sigma_i^2}}{\sum \left(\frac{1}{\sigma_i^2} \right)}$$

wherein

x is the weighted mean of the quantitative measurement;

σ_i^2 is the estimated variance of instance x_i of said quantitative measurement; and

computing said error in the mean such that,

when N approaches 1,

σ_x approaches $\sqrt{\frac{1}{\sum \left(\frac{1}{\sigma_i^2} \right)}}$

and when N approaches a large number of nominal repeats

σ_x approaches observed error from scatter in x.

132. The method of claim 131 wherein N = 4.